low-up only. The intervention consisted of eight weekly one-hour group biofeedback sessions and prescribed muscular relaxation techniques twice a day at home. Of the 107 persons assigned to the experimental group, 99 accepted the treatment, and at eight months of follow-up they had a mean reduction in blood pressure of 16.2/6.8 mm of mercury compared with 5.0/0.3 mm of mercury for the control subjects. A four-year follow-up of 86 experimental and 75 control subjects found that the effectiveness of relaxation therapy was maintained at a reduced level. The subjects who had been taught relaxation therapy had a mean reduction of 7.2/3.7 mm of mercury compared with a mean increase in the control group of 1.6/4.1 mm of mercury. Although only 14 of the 86 participants practiced relaxation at least weekly, most (63%) practiced it occasionally.

The mechanism by which relaxation therapies lower blood pressure has not been extensively studied, but may be mediated by lowering of the plasma levels of catecholamines, renin and aldosterone. Patients' expectations may also have a significant role in the effect observed with relaxation training, and a subset may exist of hyperresponsive persons who are likely to benefit. In some of the published studies, less than half of the patients were willing to continue relaxation therapy for more than a few months, and thus it is likely that in clinical practice only a minority of patients having hypertension will actually benefit.

The Health and Public Policy Committee of the American College of Physicians recently concluded that biofeedback is a second-line nonpharmacologic therapy for hypertension. Relaxation training is cheaper, easier to implement and has a greater chance for a wider application in clinical practice. Nonphysician health professionals such as nutritionists and psychologists need to be involved in implementing the nonpharmacologic management of hypertension. Teaching relaxation therapy, including the use of commercially available audiotapes, can play an important role in a multicomponent non-drug approach to treating hypertension.

ELISEO J. PÉREZ-STABLE, MD
*San Francisco*

REFERENCES

Health and Public Policy Committee, American College of Physicians: Biofeedback for hypertension. Ann Intern Med 1985 May; 102:709-715

Kaplan NM: Non-drug treatment of hypertension. Ann Intern Med 1985 Mar; 102:359-373

Patel C, Marmot MG, Terry DJ, et al: Trial of relaxation in reducing coronary risk: Four year follow-up. Br Med J 1985 Apr; 290:1103-1106

## Postprandial Hypotension

ANGINA PECTORIS AND SYNCOPE occur in some patients after large meals. In one study, a standardized breakfast for patients aged 75 to 98 years produced a mean fall in the systolic blood pressure—taken in the sitting position—of 13 mm of mercury within 35 minutes after ingesting the meal; a group of subjects aged 18 to 37 years had no significant reduction in blood pressure.

We have found that a meal produced a mean reduction in the supine diastolic blood pressure in normal subjects aged 19 to 31, associated with a reflexive increase in the mean heart rate. In patients with hypertension, a meal also reduced the mean supine diastolic blood pressure, associated with an increase in heart rate. Patients with autonomic dysfunction have a much more dramatic change in blood pressure after meals, averaging a decrease of 49 mm of mercury in the supine systolic blood pressure. Decreases as great as 98 mm of mercury have been seen.

The meal size appears to be an important determinant of hemodynamic effects, and meals with a higher protein content may have greater effects. Ingesting food increases the splanchnic blood flow and decreases total peripheral resistance, probably due to a decreased splanchnic resistance.

In many studies, elderly patients have been observed to have a greater hypotensive response to meals. In these studies, however, the blood pressure was higher in the older patients, and the magnitude of the reduction in blood pressure after the meal was also related to the premeal blood pressure.

Ingesting food lowers both systolic and diastolic blood pressures. Elderly patients, patients with hypertension and patients with autonomic insufficiency tend to have the greatest reductions in blood pressure. The hemodynamic effects of meals may contribute to postprandial syncope and to postprandial angina because of a reflex tachycardia and decreased coronary perfusion pressure. More commonly, blood pressure changes of 5 to 20 mm of mercury related to meals may contribute significantly to an apparent blood pressure lability and may seriously impair the interpretation of blood pressure control in patients with hypertension.

TIMOTHY C. FAGAN, MD
KENNETH A. CONRAD, MD
*Tucson*

REFERENCES

Fagan TC, Sawyer PR, Gourley LA, et al: Postprandial alterations in hemodynamics and blood pressure in normal subjects. Am J Cardiol 1986 Sep; 58:636-641

Lipsitz LA, Nyquist RP, Wei JY, et al: Postprandial reduction in blood pressure in the elderly. N Engl J Med 1983 Jul; 309:81-83

Robertson D, Wade D, Robertson RM: Postprandial alterations in cardiovascular hemodynamics in autonomic dysfunctional states. Am J Cardiol 1981 Dec; 48:1048-1052

## 'Unloading' Therapy for Heart Failure

VASODILATOR THERAPY can provide substantial benefits to some patients with congestive heart failure. The rationale is based on the physiologic principles of reducing ventricular afterload and preload (hence the term "unloading" therapy). This results in an increased cardiac output and decreased systemic and pulmonary venous pressures. Symptoms of hypoperfusion and congestion are ameliorated. The peripheral vascular tone (both arterial and venous) is increased in most symptomatic patients with congestive heart failure. An increased systemic vascular resistance and resistance to left ventricular ejection by arterial vasoconstriction reduces the forward stroke volume and cardiac output. Venoconstriction contributes to congestive symptoms by increasing pulmonary and systemic venous pressures; the intracardiac volume is also increased. The vasodilator drugs with predominantly arteriolar effects, such as hydralazine hydrochloride, minoxidil and nifedipine, increase cardiac output. Venodilators, such as nitroglycerin, nitrates and molsidomine, can decrease systemic and pulmonary venous pressures. Vasodilator agents with balanced arteriodilator and venodilator properties—angiotensin-converting enzyme inhibitors and $\alpha$-adrenergic blocking agents—produce hemodynamic effects similar to those of combinations of arteriodilators and venodilators.

During congestive heart failure, abnormalities of neuroendocrine function contribute to a heightened peripheral vascular tone. Elevating levels of circulatory catecholamines reflect increased sympathetic activity. Plasma renin activity is increased in about two thirds of patients who have chronic

congestive heart failure. This leads to increased production of the vasoconstrictor angiotensin II and increased release of aldosterone and norepinephrine. In some patients, arginine-vasopressin levels are also higher than normal. Vasoconstriction mediated by these neuroendocrine systems are, to some extent, counterbalanced by increased production of vasodilator prostaglandins and the vasodilator, atrial natriuretic peptide. In most symptomatic patients, however, the vasoconstrictor influences predominate, causing a net increase in systemic vascular tone.

Vasodilators have a variety of mechanisms of action. These include the following: antiadrenergic drugs ($\alpha$-receptor blocking agents, in particular), $\beta_2$-receptor agonists, vasopressin antagonists, serotonin antagonists, prostaglandins, calcium entry blocking agents, angiotensin-converting enzyme inhibitors and the direct-acting vasodilators. Hemodynamic studies using these agents usually show initially improved systemic hemodynamics and cardiac performance. Long-term clinical benefit, however, does not occur with all vasodilators. Direct-acting arteriolar vasodilators such as hydralazine or minoxidil, when used alone, do not improve the exercise capacity or clinical state significantly in patients with chronic congestive heart failure. $\alpha$-Receptor blocking agents such as prazosin hydrochloride are also ineffective in most patients. In contrast, isosorbide dinitrate and the angiotensin-converting enzyme inhibitors, captopril or enalapril maleate, improve the clinical state and exercise tolerance in most patients. Recently a Veterans Administration cooperative trial has reported that a combination of hydralazine, 300 mg a day, and isosorbide dinitrate, 160 mg a day, can improve survival of patients with mild to moderately severe chronic congestive heart failure.

Based on these reports, either a combination of hydralazine with nitrates or angiotensin-converting enzyme inhibitors should be considered in the "unloading" therapy for chronic heart failure. A lack of comparative studies prevents making a clear choice between these approaches, although correcting neuroendocrine abnormalities more effectively by using angiotensin-converting enzyme inhibitors may favor the latter.

KANU CHATTERJEE, MD
*San Francisco*

#### REFERENCES

Captopril Multi-Center Research Group: A placebo-controlled trial of captopril in refractory chronic congestive heart failure. J Am Coll Cardiol 1983; 2:755-763

Chatterjee K, Parmley WW: Vasodilator therapy for acute myocardial infarction and chronic congestive heart failure. J Am Coll Cardiol 1983 Jan; 1:133-153

Chatterjee K, Viquerat CE, Daly P: Neurohumoral abnormalities in heart failure. Heart Failure 1985 Mar-Apr; 1:69-83

Cleland JG, Dargie JH, Ball SG, et al: Effects of enalapril in heart failure: A double-blind study of effects on exercise performance, renal function, hormones and metabolic state. Br Heart J 1985 Sep; 54:305-312

Cohn JN, Archibald DG, Ziesche S, et al: Effect of vasodilator therapy on mortality in chronic congestive heart failure—Results of a Veterans Administration Cooperative Study. N Engl J Med 1986; 314:1547-1552

## Treatment of Gram-Negative Bacterial Meningitis

THE THIRD-GENERATION cephalosporin antibiotics have greatly improved the prognosis for adult patients with gram-negative bacillary meningitis. Before 1980, when aminoglycoside antibiotics and chloramphenicol were used extensively, case-fatality rates ranged from 40% to 90%. Since the third-generation cephalosporins were introduced, case-fatality rates have fallen dramatically; in fact, cure rates of 75% to 90% have become the rule. Of these agents, cefotaxime sodium and moxalactam disodium have received the most usage for this indication. Available data suggest that ceftriaxone sodium, ceftazidime and ceftizoxime sodium offer comparable efficacy. These antibiotics show potent bactericidal activity against not only *Escherichia coli* and *Klebsiella pneumoniae*, the leading pathogens, but also against many other Enterobacteriaceae. Minimum inhibitory concentrations range from 0.01 to 1.0 $\mu$g per ml for most genera of this family except *Enterobacter*. In patients with meningitis, drug concentrations in cerebrospinal fluid (CSF) greatly exceed these minimum inhibitory concentrations: peak concentrations generally range from 10 to 40 $\mu$g per ml. Thus, unlike aminoglycoside antibiotics or chloramphenicol, third-generation cephalosporins produce CSF antibiotic concentrations that are 20 to 100 times the minimum inhibitory concentration of the infecting bacterium, and they rapidly sterilize the CSF.

Despite the successes of third-generation cephalosporins, meningitis caused by certain species of gram-negative bacilli remains a difficult and somewhat controversial therapeutic problem. The most troublesome organisms include the more resistant Enterobacteriaceae, such as *Enterobacter cloacae*, as well as certain non-Enterobacteriaceae, notably *Pseudomonas aeruginosa* and *Acinetobacter calcoaceticus*. Therapy for infections caused by these organisms is optimally based on the results of quantitative susceptibility tests. As a general rule, when minimum inhibitory concentrations of the third-generation cephalosporins for the pathogen are greater than 1.0 $\mu$g per ml, patients require the most active third-generation cephalosporin or extended-spectrum penicillin plus the most active aminoglycoside antibiotic. Trimethoprim-sulfamethoxazole may be useful against some organisms, such as *A calcoaceticus*. Aminoglycoside antibiotic administration by both intravenous and intralumbar routes is recommended. Intraventricular administration through a reservoir should be considered for patients who have relapsed or responded poorly to other regimens.

LARRY J. STRAUSBAUGH, MD
*Portland, Oregon*

#### REFERENCES

Landesman SH, Corrado ML, Shah PM, et al: Past and current roles for cephalosporin antibiotics in treatment of meningitis. Am J Med 1981 Oct; 71:693-703

Mullaney DT, John JF: Cefotaxime therapy—Evaluation of its effect on bacterial meningitis, CSF drug levels and bactericidal activity. Arch Intern Med 1983 Sep; 143:1705-1708

Sande MA, Smith AL, Root RK (Eds): Contemporary Issues in Infectious Diseases—Vol. 3, Bacterial Meningitis. New York, Churchill Livingstone, 1985

## Home Intravenous Antibiotic Therapy

HOME INTRAVENOUS (IV) ANTIBIOTIC THERAPY presents an opportunity to provide hospital level therapy at a substantially lower cost while enabling patients to resume a near-normal life-style.

Proper patient selection is the cornerstone of successful home therapy. Patients appropriate for home treatment have no indications for hospital care other than the need to receive antibiotics intravenously. Common infections treated are osteomyelitis, septic arthritis, diabetic foot infections, endocarditis (after inpatient observation) or any other conditions wherein patients are medically stable except for an infection requiring IV administration of antibiotics.

Efficacy is the primary consideration for antibiotic selection in any treatment setting, but one must additionally adjust dosing times to accommodate patients' sleep patterns and use